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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,356	05/21/2002	Michael Slater	BSW-1	6283

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Ivor R Elrifi
Mintz Levin Cohn Ferris Glovsky & Popeo
One Financial Center
Boston, MA 02111

EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 07/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,356	SLATER ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-56* is/are pending in the application.

4a) Of the above claim(s) *11-13 and 34-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-10 and 19-33* is/are rejected.

7)☒ Claim(s) *14-18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ~~3/3/04+2/1/02~~. 3/3/04 KAC 7/18/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgement is made of applicant's election without traverse of Group I, and the species of P2X7.

2. Claims 1-6 and 8-56 are pending. Claims 34-56, drawn to non-elected inventions, are withdrawn from consideration. Claims 11 and 13, drawn to non-elected species are withdrawn from consideration. Claims 1-6, 8-10, 12 and 14-33 are examined on the merits.

Claim Objections

3. (a) Claims 14-18 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot serve as a basis for other multiple dependent claims. See MPEP § 608.01(n). Accordingly, the claims 14-18 not been further treated on the merits.

(b) Claim 8 is objected to because of the following informalities: the typographical error of "abody fluid". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 24-33 are rejected under 35 U.S.C. § 101 because they are not presented in the format of a proper process claim. See MPEP 2173.05(q).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 24-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 24-33, drawn to the "use of a purinergic receptor antibody," are vague an indefinite. The claims are drawn to a method of using an antibody, but fails to set forth any active, positive steps that define the claimed method. See MPEP 2173.05(q).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6, 8-11 and 19-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of staging or diagnosing cancer and a method of determining the etiology of carcinogenesis in a mammal, does not reasonably provide enablement for methods of diagnosing a pre-neoplastic state in a mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

Claims 1-6, 8-11 and 19-33 encompass the detection of cancer as well as the detection of a pre-neoplastic state. When given the broadest reasonable interpretation the detection of a pre-neoplastic state encompasses any type of cancer. The art recognizes that the P2X7 receptor is over-expressed in the lymphocytes of patients having Chronic Lymphocytic Leukemia (see 103 rejection below). The art recognizes that leukemia is a clonal disease arising from a single cell (abstract of Jacob et al, Indian J Cancer. 2002 Jun;39(2):61-5 and the abstract of Mauro et al, Curr Opin Oncol. 2001 Jan;13(1):3-7). The art (Meeker et al, Blood. 1989, Vol. 74, pp.1801-1806) teaches that the t(11;14)(q13;q32) translocation is associated with human B-lymphocytic malignancy. Thus it can be construed that a B-cell having acquired said translocation would constitute a leukemic cell. Thus, in order to carry out the claimed methods of detecting a lymphocyte which was going to progress to a leukemic cell it would necessitate that a normal B-cell would over-express the P2X7 receptor before said translocation occurred in said cell. There

is no objective evidence with in the specification or any art that this would be the case, therefore one of skill in the art would be subjected to undue experimentation without reasonable expectation of success in order to practice the broadly claimed methods.

Further, the clams encompass the detection of a pre-neoplastic state for solid tumors as well. A pre-neoplastic state in a solid organ or tissue would encompass all stages of progression to a malignant state such as hyperplasia, dysplasia and anaplasia. In order to practice the broadly claimed invention it would be necessary to detect a difference between the P2X7 expression in said cell relative to a corresponding normal cell. The specification has not taught a specific pre-neoplastic stage at which said expression would begin to deviate from the normal, nor has the specification provided evidence that any of the pre-neoplastic stages in any solid tissue or organ would exhibit a deviation in the level of expression of P2X7. Given the lack of teachings in the specification regarding all of the above issues, one of skill in the art would be subject to undue experimentation without reasonable expectation of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-3, 8-10, 19-21 and 24-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Altieri et al (WO9216558) in view of Jameison et al (Journal of Cellular Physiology, 1996, Vol. 166, pp. 637-642) and Buell et al (Blood, 1998, Vol. 92, pp. 3521-3528).

Claim 1 is drawn in part to a method of staging or diagnosing neoplastic states in a mammal, comprising detecting the P2X7 receptor expression profile of cells and/or tissues from said mammal and comparing the receptor expression profile of normal cells and/or tissues. Claim 2 is drawn to a method of determining the etiology of carcinogenesis in a mammal, comprising detecting the P2X7 receptor expression profile of cells and/or tissues from said mammal and comparing the receptor expression profile of normal cells and/or tissues. Claim 3 embodies the methods of claims 1 or 2 wherein the mammal is a human. Claim 8 embodies the methods of claims 1 or 2 wherein the cells are obtained from a body fluid. Claims 9 and 10 embody the methods of claims 1 or 2 wherein the detection of the P2X7 receptor comprises the use of an antibody reagent, and an antibody reagent specific for P2X7, respectively. Claims 19-22 embody the methods of claims 1 or 2 wherein detection of the P2X7 receptor is by immunohistochemistry, ELISA and RIA, respectively.

Altieri et al teach a method of monitoring treatment of patients afflicted with chronic lymphocytic leukemia in which expression of receptors homologous to factors V and VIII is correlated with the disease state in which the frequency of cells expressing an EPR-1 marker is inversely related to the response to treatment of patients suffering from CLL (page 36, line 3 to page 37, line 19). Altieri et al teach a method of diagnosing CLL and monitoring CLL comprising admixing a body sample containing cells to be assayed for EPR-1 marker with an instant antibody composition which specifically binds to EPR-1 and measuring the amount of immunoreaction product under predefined reaction conditions wherein the amount of immunoreaction product formed is correlated to an initial disease state (page 37, lines 21-23). Altieri et al teach that these steps are repeated at a later time during the treatment regimen thereby permitting determination of the patient's response to treatment, with a decrease in the number of EPR-1 molecules expressed on cell surfaces indicating an improvement in the disease state (page 37, lines 23-26). Altieri et al teach monoclonal and polyclonal antibodies to EPR-1 (page 25, lines 19-20 and page 26, lines 27-29), immunohistochemical, ELISA and RIA as methods to detect the EPR-1 protein (page 46, line 26 to page 47, line 23, page 39, line 32 to

page 40, line 6, page 35, lines 20-35). Altieri et al do not teach the P2X7 receptor as a marker for CLL or an antibody which binds specifically to P2X7.

Jameison et al teach that lymphocytes from patients with CLL have higher levels of P2Z receptors than the lymphocytes from normal individuals (Figure 1, and legend). The P2Z receptor is synonymous with the P2X7 receptor. Thus, the teachings of Jameison et al correlate the over-expression of the P2X7 receptor with the presence of CLL.

Buell et al teach a monoclonal antibody which specifically binds to cells which express the receptor and can be used in immunoprecipitations (pp. 3522, second column, last line to page 3224, first column, line 14).

It would have been prima facie obvious at the time the claimed invention was made to substitute the detection of the P2X7 receptor for the detection of the EPR-1 protein in the method taught by Altieri et al. One of skill in the art would have been motivated to do so by the teachings of Jamieson et al on the over-expression of P2X7 on the surface of lymphocytes from patients with CLL. One of skill in the art would understand that the P2X7 protein can serve as a marker for the disease state of CLL in the same sense as EPR-1 in that initial detection of over-expression of P2X7 is diagnostic for CLL and the decrease in the level of P2X7 in response to treatment is indicative of a positive response to treatment and a decrease in malignant lymphocytes, whereas a lack of said decrease in response to treatment would be indicative of non-responsiveness to treatment and an increase in the level of P2X7 would be indicative of the progression of CLL.

9. Claims 1-3, 8-10 and 19-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Altieri et al (WO9216558) and Jameison et al (Journal of Cellular Physiology, 1996, Vol. 166, pp. 637-642) and Buell et al (Blood, 1998, Vol. 92, pp. 3521-3528) as applied to claims 1-3, 8-10 and 19-21 and 24-34, above, and in further view of Rio et al (WO 9706256).

Claim 22 embodies the methods of claims 1 or 2 wherein the detection of the P2X7 receptor is by Western blot, and detection of P2X7 receptor mRNA. The combination of Altieri and Jameison et al and Buell et al does not specifically teach the detection of the P2X7 receptor by Western or mRNA expression.

Rio et al teach the detection of leukemia markers by Western blot and mRNA expression Page 20, lines 7-17 and page 44, lines 12-14)..

It would have been prima facie obvious at the time the claimed invention was made to use the methods of Western blot or mRNA expression for the detection of the P2X7 receptor in the method rendered obvious by the combination of Altieri et al and Jamison et al and Buell et al because the methods of Western blot and mRNA expression measurement are well known in the art and demonstrated to be useful in the detection of leukemia markers.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
7/11/2005

Karen A. Canella

KAREN A. CANELLA PH.D
PRIMARY EXAMINER